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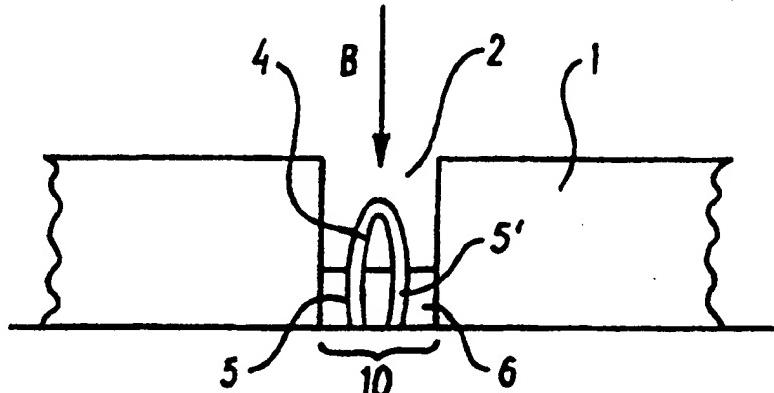
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(54) Title: MICRO-FILTRATION DEVICE

(57) Abstract

There is described a filter unit (10) which comprises a hollow fibre membrane fixed into a solid plug (6) and able to communicate with each side of the plug (6). Utilisation of the hollow fibre membrane enables a relatively large filtration area to be exposed to the sample, thus facilitating filtration. For example, the hollow fibre membranes may be in the shape of hoops (4), having their ends (5, 5') passing through the plug (6) and exposed on the far side thereof. The plug (6) is desirably formed from cured adhesive. The filter unit (10) may be located in each well (2) of a conventional filter tray (1) or may be located in the lumen of a filtration apparatus such as a pipette (11). Optionally the membrane may be treated or coated to react with a component of the sample.



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1 "Micro-filtration Device"

2

3 The present invention is concerned with the process of
4 filtration, particularly micro-filtration, and provides
5 a device capable of small volume filtration.

6

7 Filtration is a common separation technique of samples
8 and is frequently used in both chemical and biochemical
9 processes. In particular, filtration is of utility for
10 biological samples where cell debris and other organic
11 materials need to be removed. For this reason, many
12 medical diagnostic assays require a first filtration
13 step.

14

15 Generally dead-end filtration is used, in which the
16 sample is induced to pass through the filter by a
17 pressure differential, a portion of the sample being
18 retained on the filter and the remaining part of the
19 sample (the filtrate) passing through the filter and
20 being collected in a suitable chamber.

21

22 Filters may also be used as a convenient matrix on
23 which to present samples for assay purposes.

24

25 There is an increasing trend to use smaller volume

1 samples for filtration and where this is the case it is
2 usual to us a scaled-down filtration apparatus as
3 appropriate.

4

5 In such small volume filtration procedures, filtration
6 trays or pipettes are generally used. Filtration trays
7 consist of multiple open-ended wells positioned on top
8 of a single sheet of filter paper. The area of each
9 well therefore defines the area of filter available for
10 the filtering operation as the surface area of the
11 filter available for each filtration process is limited
12 to the surface area of the membrane as exposed by the
13 well. Each well can be used to filter a separate
14 sample and the whole tray can therefore be used in
15 multiple filtration operations. Typically, such
16 filtration trays consist of 24, 48 or 96 separate
17 wells, each well ending with the membrane as the lower
18 surface.

19

20 Figure 1A illustrates a cross-section of a single well
21 in a portion of a conventional micro-titre tray adapted
22 for normal use for micro-filtration processes. The
23 tray (1) contains numerous filter chambers (2) into
24 which the sample(s) are placed for filtration. Prior
25 to filtration a filter paper (3), which is essentially
26 flat, is fixed firmly to the exterior bottom surface of
27 the filtration tray (1). Once the filter paper (3) is
28 in position the sample to be filtered is poured into
29 the filter chamber (2). Optionally pressure in the
30 direction of arrow A is applied. The pressure forces
31 the sample through the filter paper (3) into a
32 collection chamber (not shown). It is clear from
33 Figure 1A that the surface area available for
34 filtration is limited to the cross-sectional area of
35 the filter chamber (2).

36

1 However, where the surface area of the filter is small
2 the filtration operation tends to suffer from the
3 following disadvantages:

4

5 1. The process of filtration may take a long time as
6 the sample has to pass through a relatively small
7 surface area of filter.

8

9 2. If biological samples are to be filtered the
10 relatively small surface area of the filter is
11 highly prone to being completely clogged with cell
12 debris, fatty deposits or other impurities.

13

14 An alternative conventional filtration operation occurs
15 using a pipette, in which a planar filter is located
16 within or on the tip of the pipette. The liquid sample
17 is taken up into the pipette by suction and is
18 filtered. A portion of the sample may be retained on
19 the filter whilst the filtrate is collected within the
20 body of the pipette. Optionally, the tip of the
21 pipette having the filter may be removable (and/or
22 optionally disposable) so that the used filter (and any
23 contaminant contained thereon) can be removed before
24 expulsion of the filtrate. The filter may be treated
25 or coated to react with or bind to a particular
26 component of the sample. An example of a pipette tip
27 having a treated membrane located thereon is the
28 Nuclitips™ DNA extraction system of Amersham Life
29 Sciences Ltd. In the Nuclitips™ pipette tip a planar
30 treated membrane is located on the exterior of the
31 pipette tip totally covering the tip's aperture, so
32 that the sample is filtered before entry into the
33 pipette tip and any DNA present in the sample binds to
34 the filter.

35

36 The present invention provides a filter unit comprising

1 a hollow fibre membrane fixed into a solid plug.

2

3 Viewed from another aspect the present invention
4 provides a membrane for a filter unit in which the
5 membrane has a greater filtration surface area than the
6 cross-sectional filtration area of the filter chamber.
7 Generally the membrane is essentially three-
8 dimensional. The membrane may have any convenient
9 shape or configuration.

10

11 The term "cross-sectional filtration area" refers to
12 the area of a cross-section of the filter chamber over
13 which filtration occurs. Normally this would be the
14 area of the floor of the filter chamber or the internal
15 diameter of a pipette lumen tip. It may be possible to
16 locate the filter part way along the length of the
17 filter chamber. If the walls of the filter chamber are
18 sloping (and therefore the cross-sectional area of the
19 filter chamber varies) the "cross-sectional filtration
20 area" is the cross-sectional area of the filter chamber
21 at the point where the filter is located.

22

23 The membrane according to the present invention is
24 fixed into a solid plug and the plug is adapted to form
25 a tight fit with the internal walls of the filter
26 chamber of interest.

27

28 It is important that part of the filter according to
29 the invention communicates with the exterior sides of
30 the plug so that the sample placed into the filter
31 chamber (and optionally subjected to pressure to urge
32 the sample across the filter) can be separated, the
33 filtrate being collected in a collection chamber placed
34 below the filtration apparatus.

35

36 In one embodiment the filter of the present invention

1 is formed from hollow fibre membranes which are wound
2 round to form a spiral. The spiral may be either two
3 dimensional, that is forms a flat coil; or may be
4 three-dimensional in which case the spiral is wound
5 upwardly into a apex.

6

7 In an alternative embodiment the filter is formed from
8 "U"-shaped hoops of hollow membrane fibres. Preferably
9 several hoops, for example over 10 hoops, especially 20
10 to 50 hoops, are present in each filter chamber.

11

12 In a yet further embodiment the filter is formed into
13 hoops as described above, but the upper portion of the
14 hoops are bent into an acute angle, thus forming an
15 inverted "V" shape. The angle may conveniently be
16 introduced into the membrane by spot application of
17 heat which welds the sides of the membrane together at
18 the point where heat is applied, thus forming a hinge.
19

20

21 In another embodiment, hollow fibre membranes each
22 having a "blind" or closed end may be used. In one
23 arrangement the blind ends may be exposed to the
24 sample. For example, multiple short lengths of hollow
25 fibres may be used, the blind end of each fibre being
26 exposed to the sample whilst the open ends are potted
27 into the plug and communicate with the filtrate
28 chamber. Conveniently the blind ended fibres diverge
29 away from a central portion of the plug into which the
30 fibres have been potted.

31

32 In an alternative embodiment using blind ended hollow
33 fibre membranes, short lengths of the fibres are cut
34 and joined together at the apex (thus closing their
35 lumens at that point) into a "teepee"-like shape. The
36 apex is exposed to the sample whilst the opposite ends
 of the membrane fibres pass through the plug and are

1 exposed on the opposite side thereof.

2

3 The filter of the present invention is located within
4 the filter chamber by means of the plug. The plug
5 forms a tight fit with the inside surfaces of the
6 filter chamber. It is essential that the plug and
7 filter chamber walls form a seal, as the sample to be
8 filtered could otherwise pass through the gap between
9 the plug and the interior of the filter chamber. The
10 filter itself is at least partially embedded within the
11 plug.

12

13 The plug will normally be formed from adhesive, usually
14 cured adhesive. Any material capable of forming a seal
15 with the membrane fibres and the filter chamber may be
16 used.

17

18 The adhesive used to form the filter plug of the
19 present invention may be any adhesive material which
20 does not react with the membrane or filter chamber
21 materials in a deleterious manner. Preferably the
22 adhesive material is quick setting, ie cures within
23 minutes, for example under 5 minutes. For certain
24 embodiments adhesive material which cures upon exposure
25 to light is particularly desirable. For example in
26 medical applications it may be preferred to use
27 adhesive which cures upon exposure to blue light,
28 especially UV light.

29

30 Suitable adhesive material is commercially available
31 and mention may be made of polymers available from
32 Ablestick Ltd (for example LCM 32, LCM 34 and LCM 35),
33 Bostick Ltd or Dynax Inc (eg 191M) as being suitable UV
34 curing adhesives.

35

36 In the invention it is essential that one portion of

1 the membrane is exposed to the unfiltered sample and
2 that another portion of the membrane communicates with
3 the collection chamber. For example, where the filter
4 is a two-dimensional spiral, the spiral will be fixed
5 into the plane of the plug, with one surface facing the
6 filter chamber and the other surface facing the
7 collection chamber. In this embodiment the filtrate
8 must undergo two filtering operations, firstly across
9 the membrane into the lumen of the hollow fibre and
10 secondly from the lumen to the collection chamber side
11 of the filter. Where the filter is in a hoop-like or
12 inverted "V" configuration, the ends of the hoop or
13 inverted "V" are located within the plug and pass
14 through the plug so that the lumen of the cut ends of
15 the hollow fibre membrane are exposed to the collection
16 chamber side of the filter apparatus. In this
17 embodiment the sample passes through the hoop or
18 inverted "V" part of the filter into the lumen thereof
19 and runs down to the ends of the lumen and out into the
20 collection chamber.

21

22 Viewed from one aspect the present invention comprises
23 a filtration device having at least one filter chamber
24 containing a hollow fibre filter potted into a solid
25 plug. The surface area of the filter is desirably
26 greater than the cross-sectional area of the filter
27 chamber floor.

28

29 Conveniently the filtration apparatus comprises
30 multiple filter chambers, each having an individual
31 filter. For example, the apparatus of the invention
32 may be a tray of any suitable material (for example
33 plastics), having multiple wells therein (eg. 24, 48 or
34 96 wells), each well being capable of being a filter
35 chamber. Alternatively, the apparatus may be in the
36 form of a pipette or a pipette tip. The filter unit is

1 sealed into the lumen of the pipette or pipette tip
2 creating an internal volume within the pipette or tip
3 which may only be accessed by the sample passing across
4 the filter. The internal volume so formed acts as the
5 filtration chamber. Following filtration of the
6 sample, the pipette tip containing the filter unit may
7 be removed, for example may be snapped off, and the
8 filtered sample may be simply expelled from the
9 pipette. Alternatively, filtrate may be expelled via
10 an alternative opening in the device or may be expelled
11 back through the original opening, passing through the
12 filter again. The pipette embodiment may also be used
13 to detect the presence of a component with the sample,
14 the component binds to the filter and is then detected.
15 The filtrate is a by-product in this embodiment. Again
16 the portion of the pipette or tip containing the filter
17 and the component of interest may be removable as
18 described above, facilitating measurement, detection or
19 further reaction thereof.

20

21 For convenience, the filter chamber and, optionally,
22 the plug as well are transparent or translucent being
23 formed from optically clear materials to enable
24 monitoring of filtration and/or the output from any
25 assay that can be measured by optical means.

26

27 The present invention also provides a process for
28 separating a sample by filtration, in which the sample
29 is passed through a filter as described above.

30

31 The membrane material may be any suitable membrane, and
32 selection of the membrane type will depend upon the
33 filtering process in question. Examples of suitable
34 membrane materials include polysulfone, cellulose,
35 cellulose diacetate and/or polypropylene. Nylon filter
36 membranes, cellulose nitrate, polytetrafluoroethylene

1 (PTFE), polyvinylidene difluoride (PVDF) and glass
2 fibres can also be used.

3

4 A wide variety of such membranes are commercially
5 available and can be bought with a range of pore sizes
6 so that selection of the filter to suit the sample can
7 be made.

8

9 The membrane is in the form of a hollow fibre and
10 desirably the internal diameter of the hollow fibre is
11 small, for example is under 2mm, especially is under
12 1mm. The internal diameter of the hollow fibre may be
13 500µm or less, for example 300µm or less.

14

15 To produce the filters according to the present
16 invention a bundle of hollow fibre membranes are taken.
17 The bundle may contain any convenient number of
18 membrane fibres, but normally will contain from 5 to 50
19 membrane fibres, for example 10 to 20 membrane fibres.
20 For example, to produce the "teepee" type of
21 arrangement the bundle of membrane fibres is welded by
22 a spot application of heat at intervals along the
23 membrane bundle. Approximately equi-distant from two
24 welds an adhesive plug is formed using adhesive,
25 preferably quick-setting adhesive, and mention may be
26 made of LCM 32 and LCM 35 of Ablestick Ltd.
27 Optionally the plug shape is predetermined either by
28 fitting a collar around the membrane bundle (and the
29 collar may be fitted either before or after the welding
30 operation has taken place) or by placing the membrane
31 bundle into a suitable mould and injecting the adhesive
32 to fill the available space. Once the adhesive is set
33 the plug is chopped in half transversely, for example
34 using a scalpel, razor blade or guillotine. Thus two
35 plugs are formed, into each of which the lumen of each
36 membrane fibre is flush with the newly created plug

1 surface. At this stage in the procedure there is
2 obtained a shortened membrane bundle having an adhesive
3 plug at each end, and approximately in the centre
4 thereof a point where the membrane fibres are welded
5 together. The weld is then cut in half and two filters
6 according to the present invention are formed. The
7 weld may be cut by use of a scalpel, guillotine or
8 razor blade.

9

10 It is also possible to modify the process so that the
11 welds are cut before the adhesive plug is cut in half
12 or even before formation of the adhesive plug. Each
13 filter formed by this process is then inserted into a
14 filter chamber by press-fitting the plug into the
15 aperture of the filter chamber. The adhesive plug and
16 the inside walls of the filter chamber form a tight
17 fit.

18

19 To form the hoop or "V" shaped filter the membrane
20 fibre bundle is first bent into a "U" shape, for
21 example bending the membrane bundle around a suitable
22 forming rod. An adhesive plug is then formed in a
23 similar manner as that described above, namely either
24 by insertion of the "U" shaped membrane bundle into a
25 suitable mould or by fitting a collar around the bundle
26 and then filling the collar or the mould with adhesive,
27 followed by curing, if necessary. The inverted "V"
28 shaped filter is formed from the hoop-shaped filter and
29 comprises the additional step of spot welding the hoop
30 at the apex so that a sharp corner is formed where the
31 heat is applied. The inverted "V" shaped filter is
32 preferable in some circumstances since this
33 configuration may be easier to insert into the filter
34 chamber.

35

36 Alternatively, the hoop or inverted "V"-shaped filter

1 may be produced by forming a shortened membrane bundle
2 with an adhesive plug at each end as described above.
3 The short ned membrane bundle may then be formed into a
4 "U"-shape and the plugs affixed together side-by-side
5 (for example by glueing) to give the required plug
6 shape. For the "V"-shaped embodiment application of
7 the heat to create the acute angle required may occur
8 either before or after the plug ends are glued together
9 to form the final plug required.

10

11 For the purpose of simple "dead-end" filtration the
12 filtration chamber will normally be located
13 substantially vertically. However, it is equally
14 possible for the filters to be used in a filtration
15 device which is arranged away from the vertical. In
16 such an embodiment it may be necessary for pressure
17 means (such as a pump, especially a suction pump) to be
18 provided in order to filter the sample.

19

20 The filters of the present invention are equally
21 applicable for a "cross-flow" filtration apparatus and
22 still provide the advantages obtained by presenting a
23 relatively large surface area in a small filtration
24 chamber.

25

26 The filters of the present application are also of use
27 as a matrix on which to present a test substance for
28 assay. The relatively large surface area of the filter
29 enables a concentration of the test substance and thus
30 amplification of the test result is possible.

31

32 The present invention will now be described with
33 reference to the drawings in which Figs. 1B to 7 show
34 configurations of the membrane within the unit and
35 Figs. 8 and 9 show one use of the unit in a pipette
36 tip. In more detail:

1 Fig. 1A illustrates a conventional filtration tray 1
2 with well 2 and filter paper 3 as discussed above.

3

4 Figure 1B illustrates a single well in a portion of a
5 filtration apparatus in the form of a filtration tray
6 having a filter of the present invention embedded in a
7 plug as described above. Figure 1B illustrates a
8 cross-section of a portion of a filtration tray 1. A
9 filter chamber 2 is illustrated and contains at the
10 bottom thereof a filter unit 10 according to the
11 invention. Unit 10 consists of a solid plug 6 which
12 forms a tight fit with the internal walls of the lumen
13 of the filter chamber 2. The plug 6 may be located in
14 the filter chamber 2 either by virtue of the resilient
15 nature of the plug 6 itself or by application of
16 adhesive between the plug 6 and the inside walls of the
17 filter chamber 2. A hollow fibre membrane is shown in
18 the form of a hoop 4, the ends 5,5' of the hoop 4 being
19 held within plug 6. For simplicity only one hoop 4 is
20 illustrated in Figure 1B although generally several
21 such hoops which may be the same, similar or of varying
22 sizes may be present each having their ends 5,5'
23 located in plug 6.

24

25 Figure 2A shows a schematic cross-section of a filter
26 unit 10 according to the present invention. The unit
27 10 illustrated in Figure 2A has a membrane in a spiral
28 configuration being either the two-dimensional coil or
29 alternatively the lower coil of the three-dimensional
30 spiral as shown in Figure 5. As illustrated in Figure
31 2A the plug 6 forms a tight fit with the internal walls
32 1,1' of the filter chamber 2. There is no gap between
33 the sides 1,1' of the filter chamber 2 and plug 6.
34 Embedded within the plug 6 is a membrane in the form of
35 a hollow fibre. The upper surface 8 of the hollow
36 fibre is exposed to the untreated sample which is added

1 into filter chamber 2. The lower surface 9 of the
2 hollow fibre is exposed from plug 6 and permits the
3 filtrate to pass through into the collection or
4 filtrat chamber (not shown).

5

6 In use a liquid sample is inserted into filter chamber
7 2. Selective filtration of the sample occurs with the
8 filtrate passing through the upper surface 8 of the
9 membrane fibre into the lumen 7 thereof. From lumen 7
10 the filtrate passes through the lower surface 9 of the
11 hollow fibre into a collection or filtrate chamber (not
12 shown). Optionally a downwardly pressure is applied
13 either by a positive pressure onto the sample in the
14 filter chamber 2 or a negative pressure from the
15 filtrate collection side, to draw the filtrate through
16 the filter unit 10.

17

18 Figure 2B illustrates an embodiment of the invention
19 when the filter unit 10 has a membrane arranged in the
20 configuration of a hoop. Again, plug 6 forms a tight
21 fit with the internal walls 1,1' of filter chamber 2.
22 In this embodiment the hollow fibre membrane is
23 positioned with its free ends 5,5' exposed on the
24 filtrate collection side of plug 6, with the main body
25 of the membrane being present in the filter chamber 2.
26 The dotted lines extend the hollow fibre upwardly into
27 the filter chamber 2 but are not drawn to scale. It is
28 also possible that instead of the filter being bent
29 into a hoop as illustrated in Figure 2B the two strands
30 come together into an apex in which the sides of the
31 fibre are spot welded together through the application
32 of heat or adhesive. In use the liquid sample is
33 placed into a filter chamber 2 and separation of the
34 sample takes place as components of the sample migrate
35 through the surface of the membrane into the lumen 7 of
36 the hollow fibre. The filtrate present in lumen 7

1 travels down the hollow fibre membrane and is collected
2 from the free ends 5,5' beneath which is located a
3 collection vessel (not shown).

4

5 In Figure 2B the free ends 5,5' of the hollow fibre
6 membrane are shown passing through plug 6 and
7 protruding therefrom. It is also possible for these
8 ends 5,5' to be flush with the lower surface of plug 6
9 and indeed for ease of manufacture of the filter unit
10 this configuration may be preferable.

11

12 Figure 3A is a top view of a membrane for a filter unit
13 according to the present invention, in the form of a
14 two-dimensional spiral. Figure 3B illustrates the side
15 view of the same membrane. The spirally arranged
16 membrane shown in Figures 3A and 3B is embedded within
17 a plug (not shown) to form a filter unit.

18

19 Figure 4 is a perspective view of a membrane for a
20 filter unit according to a further embodiment of the
21 present invention, the membrane being formed of short
22 strands of membrane fibres affixed together at the apex
23 into a "teepee" arrangement. The lower ends of each
24 membrane strand are embedded within a plug (not shown)
25 so that the lumen of each strand is free to discharge
26 filtrate into a collection chamber (not shown).

27

28 Figure 5A is a side view of a further embodiment of a
29 membrane according to the present invention in the form
30 of a three-dimensional spiral filter, with Figure 5B
31 illustrating the top view of the same membrane filter.
32 The lower portion of the spiral is embedded within a
33 plug (not shown) so that the lower end of the filter is
34 exposed on the filtrate collection side of the plug.

35

36 Figure 6 is a schematic representation of a filter unit

1 10 according to the present invention having a plug 6
2 through which the hollow fibre membrane strands are
3 each formed in the shape of a hoop 4. Multiple hoops 4
4 are present, each having their ends passing through an
5 adhesive plug 6, the lumen of each membrane strand
6 being exposed on the lower surface of the plug 6. In
7 Figure 6 four membrane fibre hoops 4 are illustrated
8 for the purpose of simplicity but it is also possible
9 for many more hoops to be present in each plug 6, for
10 example up to 20 hoops. The hoops may either be of the
11 same or similar size as illustrated in Figure 6 or may
12 be of varying sizes, that is to say the height of the
13 hoop 4 may vary. Within one preferred embodiment each
14 filter unit 10 is composed of sets of hoops 4, each
15 hoop 4 set being of different size. It is also
16 possible for the axis of each set of hoops to be
17 located in a different directions within the plug
18 relative to each other.

19

20 Figure 7 illustrates schematically a further embodiment
21 of the invention in which the filter unit 10 is formed
22 from hollow fibre membranes in the configuration of an
23 inverted "V". Again, Figure 7 only shows four such
24 strands 4' for purposes of simplicity but it may be
25 possible to have far more strands present on each plug
26 6.

27

28 Figure 8B illustrates device 11 incorporating a filter
29 unit 10 according to the invention. The filter unit 10
30 is sealed into an interior lumen of device 11, here
31 illustrated as a disposable pipette tip. The filter
32 unit 10 shown comprises plug 6 incorporating therein
33 hoops 4 of hollow fibre membrane. However, any
34 alternative filter unit 10 described above would also
35 be suitable for use in device 11.

36

1 In us a liquid sample enters through aperture 15
2 driven upwardly in the direction of the arrow by the
3 suction pressure created within the pipette apparatus
4 (shown generally in Fig. 8A). The filtrate passes
5 through the filter unit 10 as previously described into
6 the collection area 14. Optionally, components of the
7 filtrate may be localised on the upper hydrophobic
8 membrane 12 but normally hydrophobic membrane 12 is
9 used to repel the liquid sample, which may for example
10 be of an aqueous nature. The filtrate is therefore
11 prevented from entry into chamber 16 and is instead
12 retained within collection area 14.

13
14 In the Pipette embodiment illustrated in Figure 8B a
15 snap point 13 is shown which enables the lower portion
16 17 of the pipette tip to be detached from the upper
17 portion 18. Portion 17 of the tip 11 may then be
18 disposed of in situations where the components of
19 interest are located on hydrophobic membrane 12 or
20 where the filtrate sample of interest is retained
21 within storage area 14 the filtered sample can be
22 simply poured into a further vessel for easy handling
23 and/or further processing.

24
25 In a yet further embodiment the filter unit 10 may
26 retain the component of interest on the hollow fibre
27 membrane strands. The filtrate in this embodiment may
28 be of no interest and, following removal of portion 17
29 by cleavage at snap point 13, the filtrate collected in
30 storage area 14 may be thrown away and the filter unit
31 carefully washed to remove the bound sample of interest
32 located on the hollow fibre membrane.

33
34 Figure 8C illustrates an alternative device 11 also
35 containing a filter unit 10 as described above in
36 Figure 8B. Hydrophobic membrane 12 is also

1 illustrate d.

2
3 The device shown in Figure 8C comprises a non-return
4 valve 19 immediately above filter unit 10. Thus,
5 filtration of a liquid sample causes the filtrate to
6 collect in storage area 14 which is bounded by
7 hydrophobic membrane 12 and the non-return valve 19
8 immediately above filter unit 10. To expel the
9 filtrate, positive pressure is exerted by means of the
10 pipette apparatus illustrated in Figure 8A, and this
11 causes the filtrate to be expelled through aperture 22
12 of arm 20 which optionally contains a non-return valve
13 21.
14

15 Figure 9 illustrates an alternative device 11
16 containing a filter unit 10 according to the invention.
17 Filter unit 10 comprises plug 6 and hoops 4 of hollow
18 membrane fibres. Only 3 hoops are illustrated in the
19 unit 10 as shown for the purposes of simplicity. The
20 number and size of the hoops 4 may vary as required.
21 Likewise, it is possible to alter the configuration of
22 the membranes within the filter unit as required. In
23 device 11 as illustrated a primary membrane 23 covers
24 the aperture of the pipette tip. The primary membrane
25 23 serves to exclude coarse matter from the liquid
26 sample admitted into the lumen of the pipette tip, thus
27 avoiding clogging of the hollow fibre membranes by
28 large particulate matter. In the device illustrated
29 hydrophobic membrane 12 is located immediately above
30 snap point 13 and the device operates in a similar
31 manner to that described in Figure 8B.

1 CLAIMS

2

3 1. A filter unit comprising a hollow fibre membrane
4 fixed into a solid plug and able to communicate
5 with each side thereof.

6

7 2. A filter unit as claimed in Claim 1 wherein the
8 membrane has a greater filtration surface area
9 than the cross-sectional area of the plug.

10

11 3. A filter unit as claimed in either one of Claims 1
12 and 2 wherein said membrane is non-planar.

13

14 4. A filter unit as claimed in any one of Claims 1 to
15 3 wherein said plug is adapted to form a tight fit
16 with the internal walls of a filter chamber.

17

18 5. A filter unit as claimed in any one of Claims 1 to
19 4 wherein said plug is transparent or translucent.

20

21 6. A filter unit as claimed in any one of Claims 1 to
22 5 wherein said plug is formed from adhesive.

23

24 7. A filter unit as claimed in Claim 6 wherein said
25 plug is formed from UV or light curable adhesive.

26

27 8. A filter unit as claimed in any one of Claims 1 to
28 7 wherein said membrane is selected from
29 polysulphone, cellulose, cellulose diacetate,
30 polypropylene, nylon, cellulose nitrate,
31 polytetrafluoroethylene, polyvinylidene difluoride
32 and/or glass fibres.

33

34 9. A filter unit as claimed in any one of Claims 1 to
35 8 wherein the internal diameter of the hollow
36 fiber membrane is less than 2mm.

- 1 10. A filter unit as claimed in Claim 9 wherein the
2 internal diameter of the hollow fibre membrane is
3 500 μ m or less.
- 4
- 5 11. A filter unit as claimed in any one of Claims 1 to
6 10 having a single hollow fibre membrane wound
7 into a spiral configuration.
- 8
- 9 12. A filter unit as claimed in any one of Claims 1 to
10 11 having a hoop shaped hollow fibre membrane,
11 both ends of which pass through the plug and are
12 exposed on one side thereof.
- 13
- 14 13. A filter unit as claimed in Claim 12 having 20 or
15 more such hoops located in said plug.
- 16
- 17 14. A filter unit as claimed in any one of Claims 1 to
18 10 having a blind ended length of hollow fibre
19 membrane, the blind end being exposed to the
20 sample.
- 21
- 22 15. A filter unit as claimed in Claim 14 wherein the
23 blind ends diverge from each other.
- 24
- 25 16. A filter unit as claimed in any one of Claims 1 to
26 15 having a treated or coated membrane.
- 27
- 28 17. A device having a filter unit as claimed in any
29 one of Claims 1 to 16 located therein.
- 30
- 31 18. A device as claimed in Claim 17 wherein the
32 portion of said device containing said unit is
33 separable from the remainder of the device.
- 34
- 35 19. A device as claimed in either one of Claims 17 and
36 18 having a non-return valve located between said

- 1 filter unit and a collection chamber for the
2 filtrate.
- 3
- 4 20. A device as claimed in any one of Claims 17 to 19
5 having an aperture dedicated to expelling the
6 filtrate.
- 7
- 8 21. A device as claimed in any one of Claims 17 to 20
9 having multiple filter units according to any one
10 of Claims 1 to 16.
- 11
- 12 22. A process of forming a filter unit as claimed in
13 any one of Claims 1 to 16, said process comprising
14 the following steps:
- 15
- 16 a. obtaining a membrane in the form of hollow
17 fibre(s), optionally cutting said fibre(s) to
18 the required size and/or conforming said
19 fibre(s) to the required shape;
- 20
- 21 b. forming a solid plug at a required location
22 around said fibre(s); and
- 23
- 24 c. optionally trimming the ends of the fibre(s).
- 25
- 26 23. A process as claimed in Claim 22 wherein the
27 hollow fibre(s) are treated to produce a blind end
28 at one end thereof.
- 29
- 30 24. A process of filtering a sample, said process
31 comprising passing said sample through a filter
32 unit as claimed in any one of Claims 1 to 16
- 33
- 34

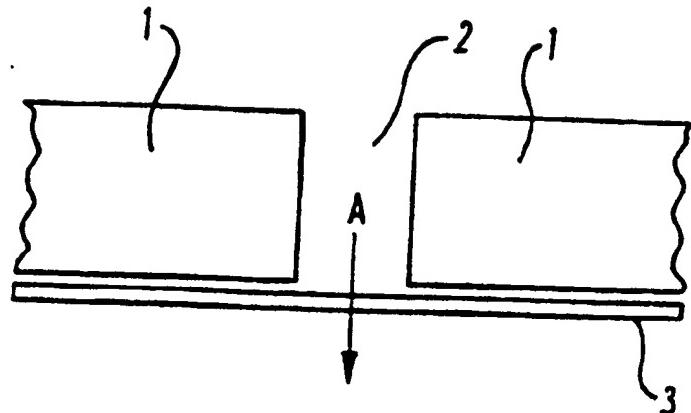
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FIG. 1A

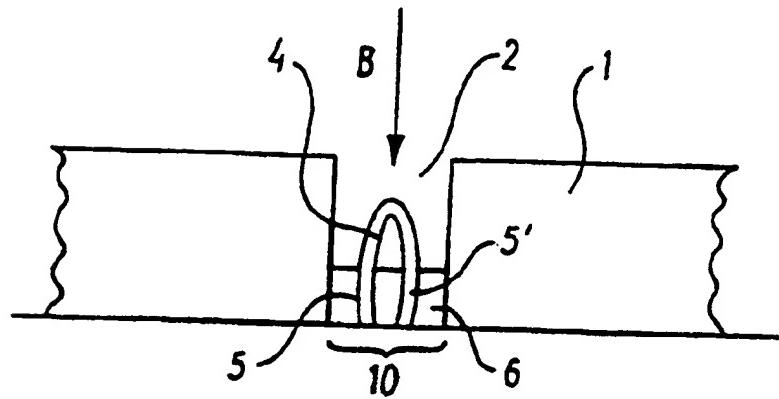


FIG. 1B

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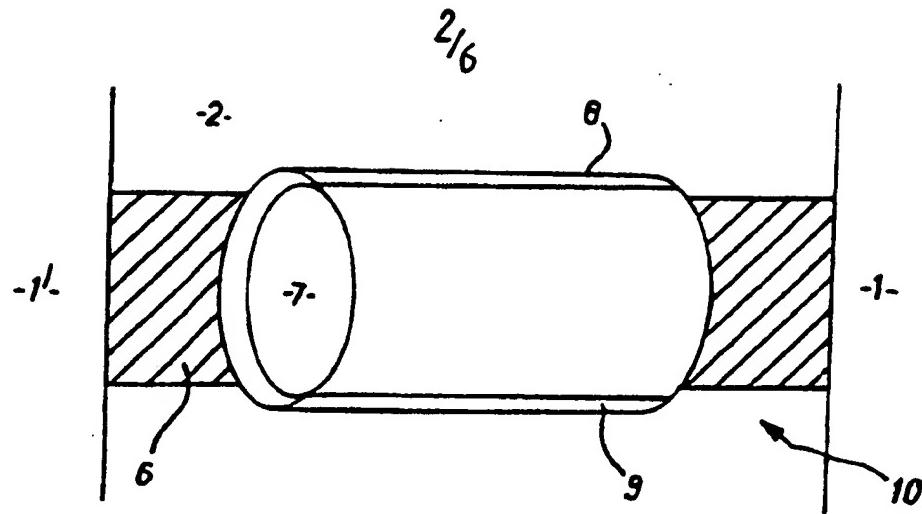


FIG. 2A

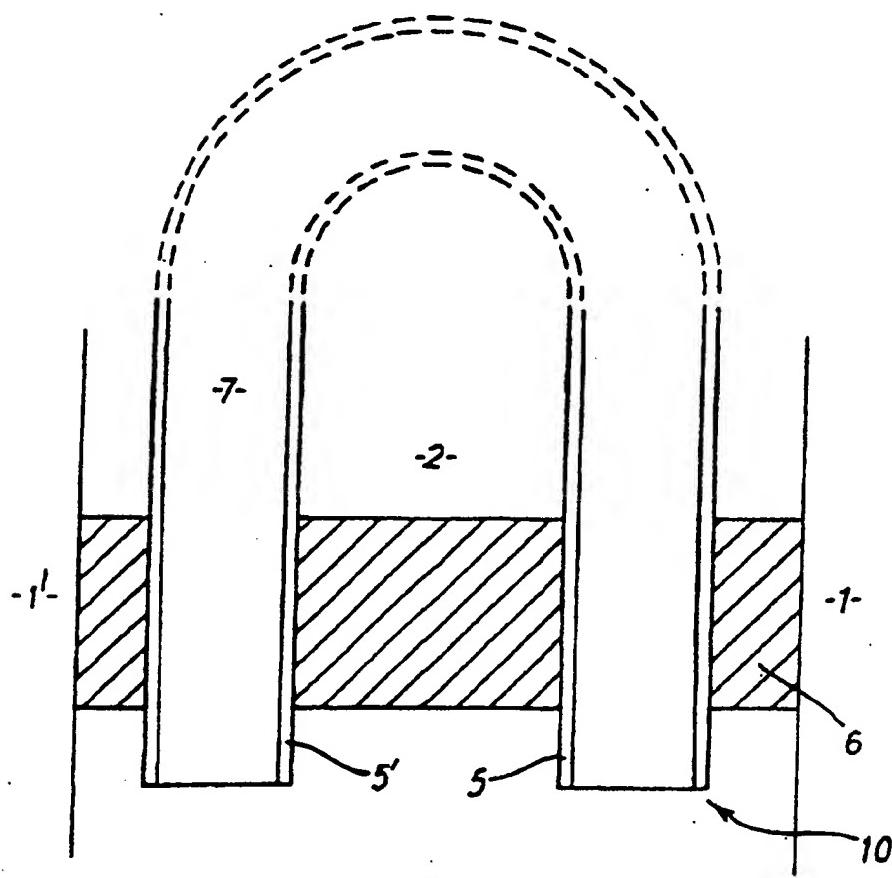


FIG. 2B

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6

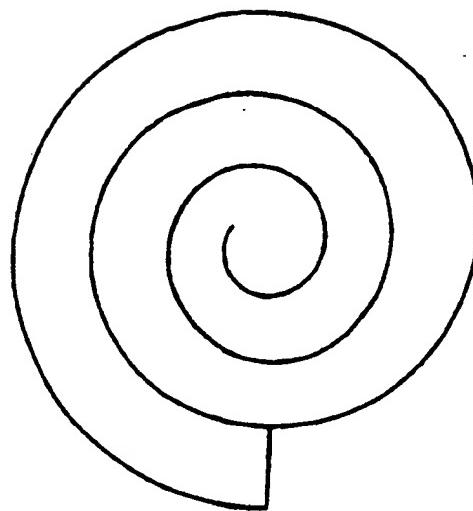


FIG.3A

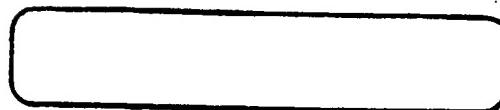


FIG.3B

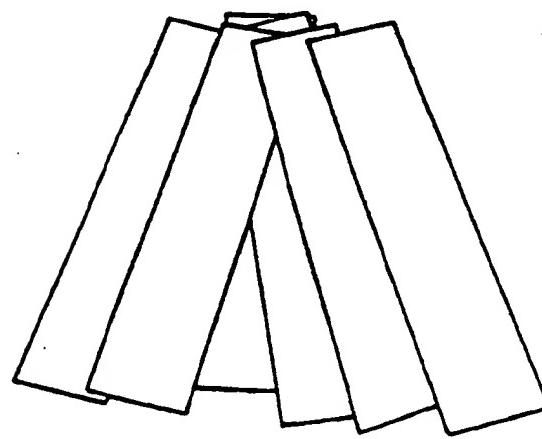


FIG.4

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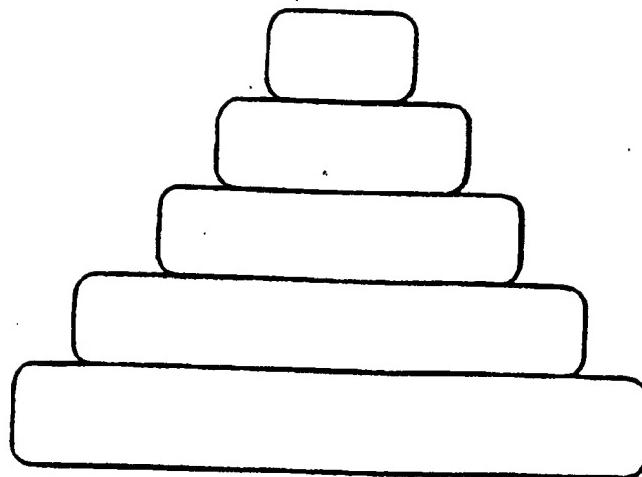


FIG.5A

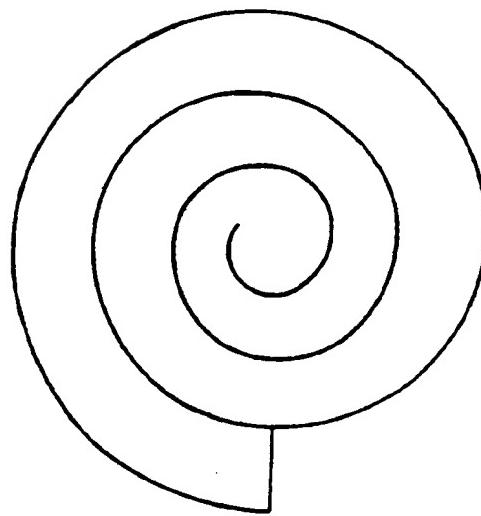


FIG.5B

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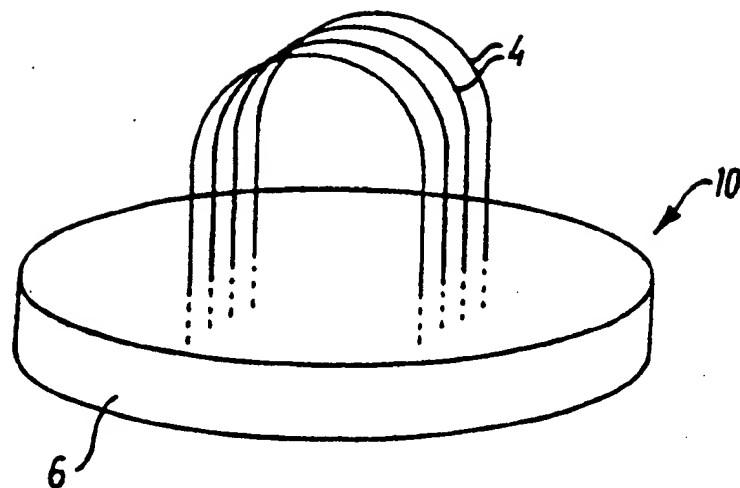


FIG.6

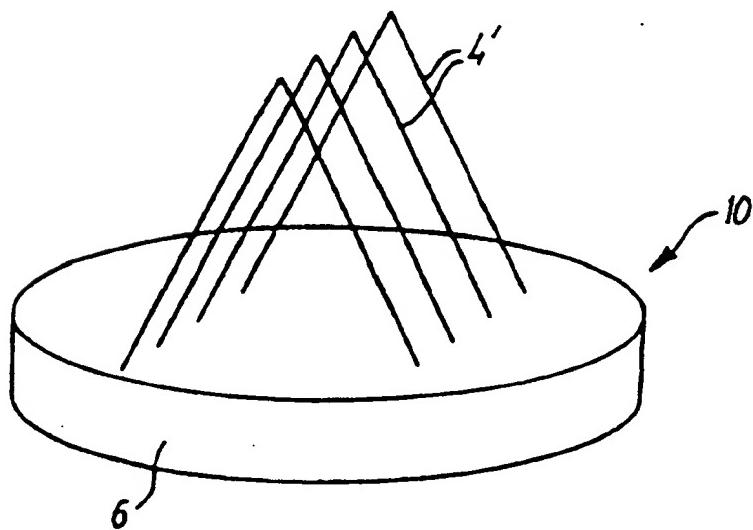
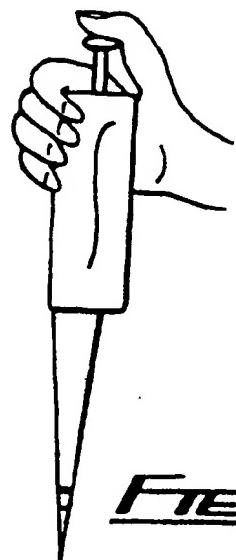
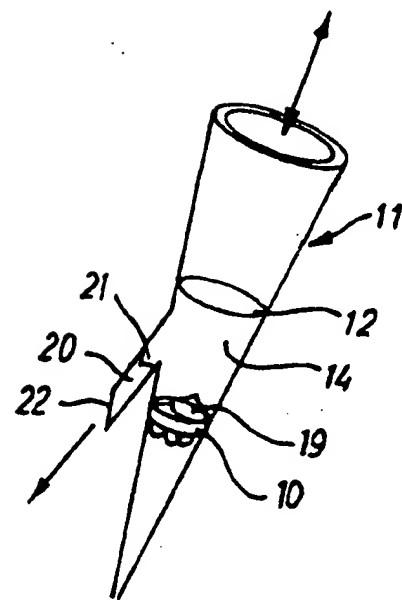
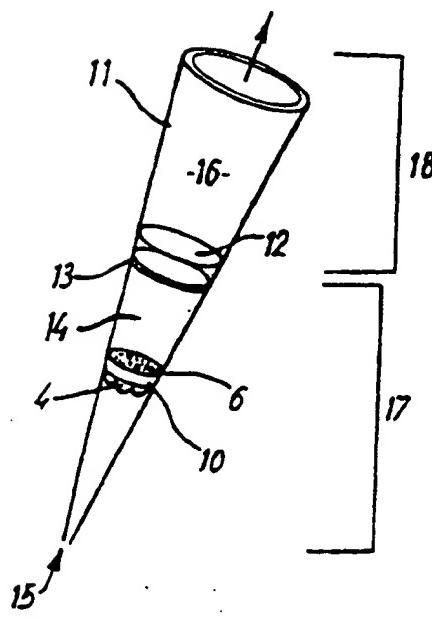
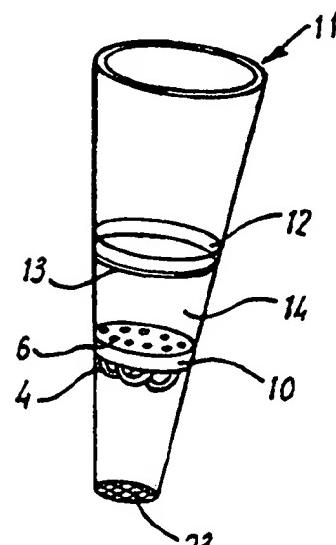


FIG.7

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FIG.8AFIG.8CFIG.8BFIG.9

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A. CLASSIFICATION F SUBJECT MATTER
IPC 6 B01D63/02 B01D61/18 B01L3/00 G01N1/40

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 B01D B01L G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PATENT ABSTRACTS OF JAPAN vol. 12 no. 344 (C-528), 16 September 1988 & JP,A,63 104615 (ASAHI CHEM IND CO LTD) 10 May 1988, see abstract	1-4, 6, 8, 9, 12-14, 17, 20, 22-24
A	& DATABASE WPI Section Ch, Week 8824 Derwent Publications Ltd., London, GB; Class A88, AN 88-165566 see abstract	5, 7, 10, 15, 16, 21
X	GB,A,2 173 711 (TOYO SODA MFG CO LTD) 22 October 1986 see the whole document	1-4, 6, 8, 9, 14, 17, 24
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Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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1

Date of the actual completion of the international search	Date of mailing of the international search report
10 April 1996	26-04- 1996

Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax (+31-70) 340-3016	Authorized officer Hoornaert, P
---	--

C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 315 252 (AKZO NV) 10 May 1989 see the whole document ---	1-4,6, 8-11,14, 17,18,24
X	US,A,5 228 992 (DEGEN) 20 July 1993 see the whole document ---	1-4,6,8, 9,12,13, 22
X	FR,A,2 393 662 (CORDIS DOW CORP) 5 January 1979 see claims 1,2,6,7; figures 2-4 see page 7, line 28 - page 8, line 1 see page 10, line 23 - page 11, line 18 ---	22
A	PATENT ABSTRACTS OF JAPAN vol. 17 no. 258 (P-1540) ,20 May 1993 & JP,A,05 002021 (KONICA CORP) 8 January 1993, see abstract & DATABASE WPI Section Ch, Week 9306 Derwent Publications Ltd., London, GB; Class B04, AN 93-049943 see abstract -----	1-4,8,17

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inventor / Application No
PCT/GB 95/02834

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
GB-A-2173711	22-10-86	JP-A-	61209010	17-09-86
		DE-A-	3608062	09-10-86
		US-A-	4690754	01-09-87
EP-A-315252	10-05-89	CA-A-	1320142	13-07-93
		DE-D-	3852375	19-01-95
		DE-T-	3852375	24-05-95
		ES-T-	2065332	16-02-95
		JP-A-	1151909	14-06-89
		US-A-	4995967	26-02-91
US-A-5228992	20-07-93	EP-A-	0559149	08-09-93
		JP-A-	5337342	21-12-93
		US-A-	5445771	29-08-95
FR-A-2393662	05-01-79	US-A-	4138460	06-02-79
		AT-B-	375837	10-09-84
		AU-B-	511941	11-09-80
		AU-B-	3656378	06-12-79
		BE-A-	868006	11-12-78
		CA-A-	1106124	04-08-81
		CH-A-	625128	15-09-81
		DE-A-	2824934	21-12-78
		GB-A-	1600448	14-10-81
		JP-C-	1311545	11-04-86
		JP-A-	54006922	19-01-79
		JP-B-	60035448	14-08-85
		NL-A-	7805968	12-12-78
		SE-B-	446305	01-09-86
		SE-A-	7806713	11-12-78